March 13, 1974

Dr. Anthony L. Schincariol
Department of Microbiology and Immunology
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Durham, North Carolina 27710

Dear Dr. Schincariol,

I am about to submit for publication a manuscript which describes some of our recent efforts to study RSV-specific DNA in normal and infected chicken cells. In most respects, our data are consistent with those presented in your recent report (Virology 56:532, 1973). However, there is one discrepancy which is of some interest to us. In Figure 10 you show 95% annealing of your PrC cDNA to DNA from uninfected chick cells. Since your cDNA is relatively representative of the RSV genome, this result could be taken to mean that virtually all of the RSV genome is present in normal cells. Surely the extensive homology (60-70%) between RAV-0 and genomes of RSV's means that a large fraction of the RSV genome should hybridize to normal cell DNA, but the issue of whether any new sequences (particularly oncogenic sequences) are added during infection is critical to attempts to decide the validity of the oncogene hypothesis. We find in experiments similar to yours, only about 30% annealing of B77 cDNA to normal chick DNA; both the rate and extent of annealing increase after infection. If the cDNA is repeatedly incubated with very large excesses of normal chick embryo DNA, as much as 50%, but no more, anneals. At this point, a considerable fraction of the remaining unannealed cDNA will, however, anneal with DNA from B77-transformed chick cells, prompting us to argue that sequences absent from normal cells are added during infection. Whether these sequences code for oncogenic functions, of course, remains to be determined.

In view of our results - and the temptation I have experienced to plot the data as a fraction of maximal annealing (rather than raw fraction hybridized) - I wonder whether you made any such correction in polting your data. If not, I suppose we can always argue ~~suppose~~ that these differences in our results may be due to sequence representation in the hybridizationpprobes, unless you have some more interesting idea.

Incidentally, I thought your paper was extremely pretty. I will send you a preprint of our less elegant manuscript.

Yours,

Harold E. Varmus, M.D.
Assistant Professor
Department of Microbiology

HEV:bb